

EDITORIAL

Sex in the CCU: women with non-ST-segment elevation acute coronary syndrome may do no worse despite less intervention

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The impact of gender on survival after an acute coronary event has been examined for decades, but still has not been resolved. Many studies have had too few women to be able to tease out the effects of age and other confounding factors, while differences in the selection of patients have led to contradictory results. Larger registry and population studies often include patients from across the spectrum of acute coronary syndrome (ACS). This makes it difficult to draw clear conclusions since the management and outcomes of ST-segment elevation acute coronary syndrome (STEACS), including ST-segment elevation myocardial infarction (STEMI) and the non-ST-segment elevation acute coronary syndrome (NSTEMACS), including non-STEMI and unstable angina, vary widely.

Two reports from European studies in this edition of *Heart* add valuable evidence to the study of gender-based outcomes of coronary artery disease. Alfredsson and his fellow authors present the findings from a large national register of Swedish patients with NSTEMACS (see article on page 1357).¹ They demonstrate that the apparently higher early mortality in women is associated with the older age at which they have coronary events. After adjustment for confounding factors, and despite less use of procedures, there was no difference in hospital mortality, or in survival at 12 months. Older women actually seemed to have better survival after discharge than men. In the second study, that from the Swiss Acute Myocardial Infarction and Unstable Angina (AMIS Plus) Registry (see article on page 1369),² female gender was not an independent predictor of in-hospital mortality after admission for ACS (60% STEACS). They also reported fewer procedures for women. These new data help to clarify some conflicting observations on outcomes for women across the spectrum of ACS.

Both studies found that women were at greater risk for in-hospital³ or 28-day⁴ mortality than men of the same age, except those over 80 years and 75 years, respectively. The difference in mortality was greatest in younger patients in both datasets. After adjustment for age, the overall hospital mortality for women on the Swedish national register was no different from that of men (odds ratio 0.98, 95% CI 0.96 to 1.00) and that was the case for women 75 years and older only in NRMI 2, but the greater risk persisted for younger women, even after adjustment for other factors including medical history and in-hospital management, and increased with decreasing age. The Swiss AMIS Plus Registry (5633 women, 58% STEMI) reported in this issue of *Heart*,² also showed higher unadjusted in-hospital mortality for women than for men in each age group. However, after adjustment for other factors this difference disappeared, except for women aged 51–60 years. Female gender was not an independent predictor of in-hospital mortality.

In contrast, this disadvantage is not evident for survival in the long term after AMI. Among the larger studies, such as that at 5 years among 25 697 patients from Ontario,⁵ and at 2 years after enrolment in the Myocardial Infarction Triage and Intervention Registry,⁶ women had similar or better adjusted survival after discharge for AMI than men. Similar outcomes at 12 months, after adjustment for age, are also reported from the very large clinical trials, such as GUSTO-I.⁷

NON-ST-SEGMENT ELEVATION ACUTE CORONARY SYNDROME (NSTEMACS)

Unlike the increased risk for death in hospital after AMI, women with NSTEMACS do not seem to be at such a great a disadvantage. In the large CRUSADE National Quality Improvement Initiative Registry⁸ from the USA with nearly 14 552 women (85% with positive cardiac markers), the adjusted odds ratio for hospital mortality was 1.01 (95% CI 0.90 to 1.13). This finding is consistent with those from smaller registries from Europe.^{9 10}

There are few long-term, gender-specific outcomes yet available from large studies of

ACUTE MYOCARDIAL INFARCTION (AMI): STEMI/STEACS/NON-STEMI

The findings from two previous registries, each with over 100 000 women with AMI, were similar. The National Registry of Myocardial Infarction 2 (NRMI 2)³ (1994–8, 55% non-Q wave AMI) and the Swedish National Acute Myocardial Infarction Register⁴ (1987–95, 89% fulfilling contemporary criteria for AMI) had sufficient numbers to examine closely mortality within age and sex

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Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; NSTEMACS, non-ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; RIKS-HIA, Register of Information and Knowledge about Swedish Heart Intensive Care Admissions; STEACS, ST-segment elevation acute coronary syndrome; STEMI, ST-segment elevation myocardial infarction

NSTEACS. Among the larger cohorts of women in clinical trials, no difference in hospital mortality or 12 month survival was reported for the 4836 women randomised in the CURE trial¹¹ of clopidogrel and aspirin.

Findings from the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA) published in this edition of *Heart*¹ provide information on the outcomes for almost 20 000 women from a national database of 53 781 patients with non-STEMI (72%) and unstable angina. The adjusted odds for in-hospital and 30-day mortality showed no difference in outcome between men and women. At 12 months, a survival benefit in favour of women was found. The RIKS-HIA database adds value for the future assessment of the effect of gender on outcomes, as repeated record linkage to national hospitalisation and death registers will allow this cohort to be re-evaluated over the longer term.

ROLE OF REVASCULARISATION PROCEDURES

Excess adjusted in-hospital mortality for women after coronary artery bypass graft surgery has been a consistent finding, even with falling surgical mortality.¹² In contrast, population-based studies show that age-adjusted, long-term survival for women after coronary artery bypass equals, or exceeds, that of men.^{13 14}

The New York State database of over 100 000 cases of percutaneous coronary intervention (PCI)¹⁵ undertaken between 1999 and 2001 demonstrated low hospital mortality overall (0.3% for men vs 0.6% for women). After adjustment for clinical variables, women remained at greater risk for in-hospital death at all ages. Other large observational studies, however, have found equivalent adjusted hospital mortality after PCI for women and men,¹⁶ and this was the case for the Swiss AMIS Plus Registry.²

Few large studies of long-term survival after PCI have been published. At 3 years the adjusted hazard mortality was 0.78 (95% CI 0.620 to 0.969) for 1331 women from three hospitals in New York State.¹⁷

SUMMARY OF SURVIVAL OUTCOMES

Worse hospital mortality for women with STEMI is a consistent finding, even after adjustment for age and other confounders. This is especially so for younger women, so concern is warranted given rising population levels of obesity and diabetes in developed countries.

The results from the RIKS-HIA study, like those from CRUSADE, suggest that women with NSTEMI are not at the same disadvantage. Even the early apparently higher mortality in younger women with NSTEMI has been shown by Alfredsson *et al* to be due to confounding factors.

After discharge for a coronary event women do at least as well as men, and with passing time the natural advantage in longevity that women enjoy seems to prevail, despite a higher use of revascularisation procedures in men.

The equality in outcomes for women with NSTEMI is against a background, almost universally reported, of reduced access to more aggressive early interventions, which persists and is confirmed in both the Swedish RIKS-HIA and the Swiss AMIS Plus studies. The assumption that mortality across the spectrum of ACS would improve with greater access to early intervention for women may be wrong. Early intervention carries with it an increased risk for mortality and for periprocedural myocardial damage,¹⁸ and this hazard is more pronounced in women.¹⁹ For lower-risk cases, which more frequently are women, the benefits of a measured response, previously characterised as an access problem,¹⁹ may outweigh the risks.

There is still much to be understood about women with coronary artery disease, their outcomes relative to men and their response to early intervention. Large national studies of unselected patients such as RIKS-HIA and AMIS Plus are excellent platforms for the study of outcomes of ACS, and can highlight disparities in outcomes and treatments and assess the impact on survival.

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